

## **Modeling Diseases in NCI Thesaurus: Initial Model with Examples**

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### **Goals**

This model of neoplasms and related diseases addresses two basic needs:

1. To define, code, and retrieve neoplasms according to their essential aspects and criteria; and
2. To represent known but weaker associations – such as normal, indicative, and experimentally associated findings – important for both clinical and research purposes.

Definitional aspects are most important, both to our understanding of cancer and to ensure the logical integrity of disease concepts. How much non-definitional data can and should go in the terminology remains an open question.

### **Relating Disease Concepts to Defining and Associated Features**

**Defining roles** for neoplasms are criteria used to make the diagnosis. Such assertions should hold true for all subtypes, so inherited values remain valid; values will often be more narrowly restricted for particular subtypes. Initial defining roles:

All*	Disease_Has_Associated_Anatomic_Site	<Anatomy>
All	Disease_Has_Primary_Anatomic_Site	<Anatomy>
All	Disease_Has_Metastatic_Anatomic_Site	<Anatomy>
All	Disease_Has_Normal_Tissue_Origin	<Anatomy: Tissue>
All*	Disease_Has_Normal_Cell_Origin	<Anatomy: Normal Cell>
All	Disease_Has_Abnormal_Cell	<Abnormal Cell>
All	Disease_Has_Molecular_Abnormality	<Molecular Abnormality>
All	Disease_Has_Cytogenetic_Abnormality	<Molecular Abnormality: Cytogenetic Abnormality>
All	Disease_Has_Finding	<Findings and Disorders: Finding>
All	Disease_Is_Stage	<Property/Attribute: Disease Stage Modifier>
All	Disease_Is_Grade	<Property/Attribute: Disease Grade Modifier>

\* “Some” may be needed in Apelon software for mixed values (e.g. associated sites for metastases, normal tissue/cell of mixed tumors).

**Non-defining roles** for neoplasms reflect significant associations which are not true for all instances. This is indicated in the logic by the “Some” qualifier, and to users by the “May\_Have” role names. Inherited values should still remain broadly true; if *some* becomes *none* for some subtypes, it is preferable to assert only at subtype level (availability of negation could change this).

Some	Disease_May_Have_Normal_Tissue_Origin	<Anatomy: Tissue>
Some	Disease_May_Have_Normal_Cell_Origin	<Anatomy: Normal Cell>
Some	Disease_May_Have_Abnormal_Cell	<Abnormal Cell>
Some	Disease_May_Have_Molecular_Abnormality	<Molecular Abnormality>
Some	Disease_May_Have_Cytogenetic_Abnormality	<Molecular Abnormality: Cytogenetic Abnormality>
Some	Disease_May_Have_Finding	<Findings and Disorders: Finding>
Some	Disease_May_Have_Associated_Disease	<Findings and Disorders: Diseases and Disorders>

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### Lymphoma Examples Applying the Model

Note: Only select concepts and roles/values are shown, to illustrate various aspects.  
Roles/values are shown only where introduced, and inherit down.

- 1 Lymphoma
  - 1.1 Hodgkin's Lymphoma
    - 1.1.1 Nodular Lymphocyte Predominant Hodgkin's Lymphoma
  - 1.2 Mature B-Cell Non-Hodgkin's Lymphoma
    - 1.2.1 Mantle Cell Lymphoma
    - 1.2.2 Diffuse Large B-Cell Lymphoma (DLBCL)
      - 1.2.2.1 Diffuse Large B-Cell Lymphoma with a Germinal Center B-Cell Expression Profile (GCB-DLBCL)
      - 1.2.2.2 Diffuse Large B-Cell Lymphoma with an Activated B-Cell Expression Profile (ABC-DLBCL)
      - 1.2.2.3 Centroblastic Lymphoma
      - 1.2.2.4 Immunoblastic Lymphoma

#### 1 Lymphoma

All	Disease_Has_Primary_Anatomic_Site	Organ System
All	Disease_Has_Normal_Cell_Origin	Lymphocyte
All	Disease_Has_Abnormal_Cell	Neoplastic Lymphocyte

#### 1.1 Hodgkin's Lymphoma

[one or other value]

Some	Disease_Has_Normal_Cell_Origin	B-Cell [omit or children only]
Some	Disease_Has_Normal_Cell_Origin	T-Cell [omit or children only]

#### 1.1.1 Nodular Lymphocyte Predominant Hodgkin's Lymphoma

[inherits from Hodgkin's Lymphoma above, but 100% B-Cell]

All	Disease_Has_Normal_Cell_Origin	B-Cell
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#### 1.2 Mature B-Cell Non-Hodgkin's Lymphoma

All	Disease_Has_Normal_Cell_Origin	Mature B-Cell
All	Disease_Has_Molecular_Abnormality	Clonal Immunoglobulin Heavy Chain Gene Rearrangement
All	Disease_Has_Molecular_Abnormality	Clonal Immunoglobulin Light Chain Gene Rearrangement

#### 1.2.1 Mantle Cell Lymphoma

All	Disease_Has_Primary_Anatomic_Site	Lymphatic System
All	Disease_Has_Normal_Tissue_Origin	Mantle Zone
All	Disease_Has_Normal_Cell_Origin	Mature B-Lymphocyte
All	Disease_Has_Abnormal_Cell	Centrocyte
All	Disease_Has_Cytogenetic_Abnormality	t(11;14)(q13;q32) Chromosomal Translocation
All	Disease_Has_Molecular_Abnormality	Monoclonal BCL-1 Gene Rearrangement
All	Disease_Has_Molecular_Abnormality	Cyclin D1 mRNA Overexpression

[most patients:]

Some	Disease_May_Have_Finding	Lymphadenopathy
Some	Disease_May_Have_Finding	Hepatomegaly
Some	Disease_May_Have_Finding	Splenomegaly

[none or one of:]

Some	Disease_May_Have_Cytogenetic_Abnormality	Trisomy 12
Some	Disease_May_Have_Cytogenetic_Abnormality	del(13q14)
Some	Disease_May_Have_Cytogenetic_Abnormality	del(17p)

### 1.2.2 Diffuse Large B-Cell Lymphoma (DLBCL)

All	Disease_Has_Finding	Rapidly Enlarging Mass
All	Disease_Has_Morphologic_Finding	Diffuse Pattern

#### 1.2.2.1 Diffuse Large B-Cell Lymphoma with a Germinal Center B-Cell Expression Profile (GCB-DLBCL)

All	Disease_Has_Finding	Favorable Clinical Outcome
All	Disease_Has_Cytogenetic_Abnormality	t(14;18)(q32;q21)
All	Disease_Has_Molecular_Abnormality	BCL-6 Gene Expression
All	Disease_Has_Molecular_Abnormality	LMO2 Gene Expression
All	Disease_Has_Molecular_Abnormality	A-myb Gene Expression
Some	Disease_May_Have_Normal_Cell_Origin	Large Non-Cleaved Cell (Centroblast)
Some	Disease_May_Have_Normal_Cell_Origin	B-Immunoblast
Some	Disease_May_Have_Abnormal_Cell	Neoplastic Large Non-Cleaved Cell (Neoplastic Centroblast)
Some	Disease_May_Have_Abnormal_Cell	Neoplastic B-Immunoblast
Some	Disease_May_Have_Abnormal_Cell	Multilobated Neoplastic B Lymphocyte

#### 1.2.2.2 Diffuse Large B-Cell Lymphoma with an Activated B-Cell Expression Profile (ABC-DLBCL)

All	Disease_Has_Normal_Cell_Origin	Memory B-Lymphocyte
All	Disease_Has_Finding	Aggressive Clinical Course
All	Disease_Has_Molecular_Abnormality	Increased NFkappa Pathway Activation
All	Disease_Has_Molecular_Abnormality	BCL-2 Gene Expression
All	Disease_Has_Molecular_Abnormality	CD44 Gene Expression
Some	Disease_May_Have_Normal_Cell_Origin	Large Non-Cleaved Cell (Centroblast)
Some	Disease_May_Have_Normal_Cell_Origin	B-Immunoblast
Some	Disease_May_Have_Abnormal_Cell	Neoplastic Large Non-Cleaved Cell (Neoplastic Centroblast)
Some	Disease_May_Have_Abnormal_Cell	Neoplastic B-Immunoblast

#### 1.2.2.3 Centroblastic Lymphoma

All	Disease_Has_Abnormal_Cell	Neoplastic Large Non-Cleaved Cell (Neoplastic Centroblast)
All	Disease_Has_Finding	Aggressive Clinical Course

#### 1.2.2.4 Immunoblastic Lymphoma

All	Disease_Has_Abnormal_Cell	Neoplastic B-Immunoblast ( $\geq 90\%$ )
All	Disease_Has_Finding	Aggressive Clinical Course

## **Myelodysplastic Syndrome Examples**

### **Myelodysplastic Syndrome**

All Disease\_Has\_Associated\_Anatomic\_Site Bone Marrow  
All Disease\_Has\_Associated\_Anatomic\_Site Blood  
All Disease\_Has\_Primary\_Anatomic\_Site Bone Marrow  
All Disease\_Has\_Normal\_Cell\_Origin Bone Marrow Stem Cell  
All Disease\_Has\_Abnormal\_Cell Clonal Hematopoietic Stem Cell  
All Disease\_Has\_Finding Ineffective Hematopoiesis Present  
All Disease\_Has\_Finding Bone Marrow Dysplasia Present  
All Disease\_Has\_Finding Myeloblasts Under 20 Percent of Bone Marrow Nucleated Cells  
All Disease\_Has\_Finding Myeloblasts Under 20 Percent of Peripheral Blood White Cells

#### **Refractory Anemia**

All Disease\_Has\_Abnormal\_Cell Dysplastic Erythroblast  
Some Disease\_May\_Have\_Abnormal\_Cell Megaloblast  
Some Disease\_May\_Have\_Abnormal\_Cell Ringed Sideroblast  
All Disease\_Has\_Finding Myeloblasts Under 1 Percent of Peripheral Blood White Cells  
All Disease\_Has\_Finding Myeloblasts Under 5 Percent of Bone Marrow Nucleated Cells  
All Disease\_Has\_Finding Ringed Sideroblasts Under 15 Percent of Erythroid Precursors  
Some Disease\_May\_Have\_Finding Hypercellular Bone Marrow  
Some Disease\_May\_Have\_Finding Anisocytosis  
Some Disease\_May\_Have\_Finding Poikilocytosis  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality del(20q)  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 8  
All Disease\_Is Low Risk

#### **Refractory Anemia with Ringed Sideroblasts**

All Disease\_Has\_Abnormal\_Cell Dysplastic Erythroblast  
All Disease\_Has\_Abnormal\_Cell Ringed Sideroblast  
Some Disease\_May\_Have\_Abnormal\_Cell Megaloblast  
All Disease\_Has\_Finding Ringed Sideroblasts 15 Percent or More of Erythroid Precursors  
All Disease\_Has\_Finding Myeloblasts Under 5 Percent of Bone Marrow Nucleated Cells  
Some Disease\_May\_Have\_Finding Anisochromasia  
Some Disease\_May\_Have\_Finding Hypercellular Bone Marrow  
Some Disease\_May\_Have\_Finding Hemosiderin-Laden Macrophage  
All Disease\_Is Low Risk

#### **Refractory Cytopenia with Multilineage Dysplasia**

Some Disease\_May\_Have\_Abnormal\_Cell Dysplastic Erythroblast  
Some Disease\_May\_Have\_Abnormal\_Cell Large Multinucleated Erythroid Cell  
Some Disease\_May\_Have\_Abnormal\_Cell Megaloblast  
Some Disease\_May\_Have\_Abnormal\_Cell Dysplastic Granulocyte  
Some Disease\_May\_Have\_Abnormal\_Cell Dysplastic Neutrophil  
Some Disease\_May\_Have\_Abnormal\_Cell Neutrophil with Pseudo Pelger-Huet Nucleus  
Some Disease\_May\_Have\_Abnormal\_Cell Hypolobated Megakaryocyte  
Some Disease\_May\_Have\_Abnormal\_Cell Micromegakaryocyte  
All Disease\_Has\_Finding Bone Marrow Dysplasia Present in 10 Percent or More of the Cells of Two Cell Lines  
All Disease\_Has\_Finding Myeloblasts Under 5 Percent of Bone Marrow Nucleated Cells  
All Disease\_Has\_Finding Myeloblasts Under 1 Percent of Peripheral Blood White Cells  
Some Disease\_May\_Have\_Finding Neutropenia  
Some Disease\_May\_Have\_Finding Thrombocytopenia  
Some Disease\_May\_Have\_Finding Trisomy 8  
Some Disease\_May\_Have\_Finding Monosomy 7  
Some Disease\_May\_Have\_Finding del(7q)  
Some Disease\_May\_Have\_Finding Monosomy 5  
Some Disease\_May\_Have\_Finding del(20q)  
All Disease\_Is High Risk

#### **Refractory Cytopenia with Multilineage Dysplasia and Ringed Sideroblasts**

All Disease\_Has\_Finding Ringed Sideroblasts 15 Percent or More of Erythroid Precursors

#### **Refractory Anemia with Excess Blasts**

Some Disease\_May\_Have\_Abnormal\_Cell Dysplastic Erythroblast  
Some Disease\_May\_Have\_Abnormal\_Cell Large Multinucleated Erythroid Cell  
Some Disease\_May\_Have\_Abnormal\_Cell Megaloblast  
Some Disease\_May\_Have\_Abnormal\_Cell Dysplastic Granulocyte  
Some Disease\_May\_Have\_Abnormal\_Cell Dysplastic Neutrophil  
Some Disease\_May\_Have\_Abnormal\_Cell Neutrophil with Pseudo Pelger-Huet Nucleus  
Some Disease\_May\_Have\_Abnormal\_Cell Neutrophil with Pseudo Chediak-Higashi Granules  
Some Disease\_May\_Have\_Abnormal\_Cell Hypolobated Megakaryocyte

Some Disease\_May\_Have\_Abnormal\_Cell Micromegakaryocyte  
 Some Disease\_May\_Have\_Finding Myeloblasts 5-19 Percent of Bone Marrow Nucleated Cells [Note RAEB-2 exceptional cases]  
 Some Disease\_May\_Have\_Finding Neutropenia  
 Some Disease\_May\_Have\_Finding Thrombocytopenia  
 Some Disease\_May\_Have\_Finding Anisopoikilocytosis  
 Some Disease\_May\_Have\_Finding Abnormal Platelet  
 Some Disease\_May\_Have\_Finding Hypercellular Bone Marrow  
 Some Disease\_May\_Have\_Finding Hypocellular Bone Marrow  
 Some Disease\_May\_Have\_Finding del(20q)  
 Some Disease\_May\_Have\_Finding del(7q)  
 Some Disease\_May\_Have\_Finding Gain of Chromosome 8  
 Some Disease\_May\_Have\_Finding Monosomy 5  
 All Disease\_Is High Risk

#### **RAEB-1**

All Disease\_Has\_Finding Myeloblasts 5-9 Percent of Bone Marrow Nucleated Cells  
 All Disease\_Has\_Finding Myeloblasts Under 5 Percent of Peripheral Blood White Cells

#### **RAEB-2** [Note: Either the 1<sup>st</sup> is true, or in rare cases conditions 2 and 3 are true:]

Some Disease\_May\_Have\_Finding Myeloblasts 10-19 Percent of Bone Marrow Nucleated Cells  
 Some Disease\_May\_Have\_Finding Myeloblasts Under 10 Percent of Bone Marrow Nucleated Cells  
 Some Disease\_May\_Have\_Finding Myeloblasts 5-19 Percent of Peripheral Blood White Cells  
 Some Disease\_May\_Have\_Finding Auer Rods Present

#### **Myelodysplastic Syndrome Associated with Isolated del(5q) Chromosome Abnormality**

All Disease\_Has\_Abnormal\_Cell Dysplastic Erythroblast  
 Some Disease\_May\_Have\_Abnormal\_Cell Hypolobated Megakaryocyte  
 All Disease\_Has\_Finding Myeloblasts Under 5 Percent of Bone Marrow Nucleated Cells  
 All Disease\_Has\_Finding Myeloblasts Under 5 Percent of Peripheral Blood White Cells  
 Some Disease\_May\_Have\_Finding Leukopenia  
 Some Disease\_May\_Have\_Finding Thrombocytosis  
 Some Disease\_May\_Have\_Finding Hypercellular Bone Marrow  
 Some Disease\_May\_Have\_Finding Megakaryocytes Increased  
 All Disease\_Has\_Finding del(5q)  
 All Disease\_Is Low Risk

#### **Myelodysplastic Syndrome, Unclassifiable**

Some Disease\_May\_Have\_Abnormal\_Cell Dysplastic Granulocyte  
 Some Disease\_May\_Have\_Abnormal\_Cell Dysplastic Neutrophil  
 Some Disease\_May\_Have\_Abnormal\_Cell Dysplastic Megakaryocyte  
 All Disease\_Has\_Finding Myeloblasts Under 5 Percent of Bone Marrow Nucleated Cells  
 All Disease\_Has\_Finding Myeloblasts Under 1 Percent of Peripheral Blood White Cells  
 Some Disease\_May\_Have\_Finding Neutropenia  
 Some Disease\_May\_Have\_Finding Thrombocytopenia  
 Some Disease\_May\_Have\_Finding Hypercellular Bone Marrow  
 Some Disease\_May\_Have\_Finding Hypocellular Bone Marrow

#### **de novo Myelodysplastic Syndrome**

Some Disease\_May\_Have\_Finding Benzene Exposure

#### **Secondary Myelodysplastic Syndrome**

##### **Therapy-Related Myelodysplastic Syndrome**

##### **Epipodophyllotoxin-Related Myelodysplastic Syndrome**

##### **Alkylating Agent-Related Myelodysplastic Syndrome**

Some Disease\_May\_Have\_Abnormal\_Cell Dysplastic Erythroblast  
 Some Disease\_May\_Have\_Abnormal\_Cell Dysplastic Granulocyte  
 Some Disease\_May\_Have\_Abnormal\_Cell Dysplastic Neutrophil  
 Some Disease\_May\_Have\_Abnormal\_Cell Dysplastic Megakaryocyte  
 Some Disease\_May\_Have\_Finding Ringed Sideroblasts 15 Percent or More of Erythroid Precursors  
 Some Disease\_May\_Have\_Finding Auer Rods Present  
 Some Disease\_May\_Have\_Finding Pancytopenia  
 Some Disease\_May\_Have\_Finding Neutropenia  
 Some Disease\_May\_Have\_Finding Thrombocytopenia  
 Some Disease\_May\_Have\_Finding Hypercellular Bone Marrow  
 Some Disease\_May\_Have\_Finding Hypocellular Bone Marrow  
 Some Disease\_May\_Have\_Finding Bone Marrow Basophilia  
 Some Disease\_May\_Have\_Finding Bone Marrow Fibrosis  
 All Disease\_Is High Risk

#### **Previously Treated Myelodysplastic Syndrome**

## **Epithelial Hepatic and Intrahepatic Bile Duct Examples**

### **Epithelial Hepatic and Intrahepatic Bile Duct Neoplasm**

All Disease\_Has\_Associated\_Anatomic\_Site Gastrointestinal System

All Disease\_Has\_Primary\_Anatomic\_Site Gastrointestinal System

All Disease\_Has\_Normal\_Cell\_Origin Epithelial Cell

All Disease\_Has\_Abnormal\_Cell Neoplastic Epithelial Cell

### **Liver and Intrahepatic Biliary Tract Carcinoma**

All Disease\_Has\_Abnormal\_Cell Malignant Epithelial Cell

#### **Hepatocellular Carcinoma**

All Disease\_Has\_Associated\_Anatomic\_Site Liver

All Disease\_Has\_Primary\_Anatomic\_Site Liver

All Disease\_Has\_Normal\_Tissue\_Origin Hepatic Tissue

All Disease\_Has\_Normal\_Cell\_Origin Hepatocyte

All Disease\_Has\_Abnormal\_Cell Adenocarcinoma Cell

Some Disease\_May\_Have\_Abnormal\_Cell Pleomorphic Adenocarcinoma Cell

Some Disease\_May\_Have\_Abnormal\_Cell Adenocarcinoma Spindle Cell

Some Disease\_May\_Have\_Abnormal\_Cell Giant Adenocarcinoma Cell

Some Disease\_May\_Have\_Abnormal\_Cell Adenocarcinoma Clear Cell

Some Disease\_May\_Have\_Abnormal\_Cell Poorly Differentiated Adenocarcinoma Cell

Some Disease\_May\_Have\_Abnormal\_Cell Polygonal Adenocarcinoma Cell with Eosinophilic Cytoplasm

Some Disease\_May\_Have\_Abnormal\_Cell Adenocarcinoma Cell with Eosinophilic Granular Cytoplasm

Some Disease\_May\_Have\_Finding Abdominal Pain

Some Disease\_May\_Have\_Finding Malaise

Some Disease\_May\_Have\_Finding Weight Loss

Some Disease\_May\_Have\_Finding Hepatomegaly

Some Disease\_May\_Have\_Finding Ascites

Some Disease\_May\_Have\_Finding Splenomegaly

Some Disease\_May\_Have\_Finding Fever

Some Disease\_May\_Have\_Finding Jaundice

Some Disease\_May\_Have\_Finding Aspartate Aminotransferase Increased

Some Disease\_May\_Have\_Finding Alanine Aminotransferase Increased

Some Disease\_May\_Have\_Finding Gamma Glutamyltransferase Increased

Some Disease\_May\_Have\_Finding Alpha Fetoprotein Increased

Some Disease\_May\_Have\_Finding Trabecular Pattern

Some Disease\_May\_Have\_Finding Pseudoglandular Pattern

Some Disease\_May\_Have\_Finding Acinar Pattern

Some Disease\_May\_Have\_Finding Compact Pattern

Some Disease\_May\_Have\_Finding Schirrous Pattern

Some Disease\_May\_Have\_Finding Fatty Change

Some Disease\_May\_Have\_Finding Mallory Body

Some Disease\_May\_Have\_Finding Ground Glass Nuclear Inclusion

Some Disease\_May\_Have\_Finding Globular Hyaline Body

All Disease\_Has\_Molecular\_Abnormality Monoclonal Hepatocyte Population

Some Disease\_May\_Have\_Molecular\_Abnormality P53 Tumor-Suppressor Gene Inactivation

Some Disease\_May\_Have\_Molecular\_Abnormality CCND1 Gene Amplification

Some Disease\_May\_Have\_Molecular\_Abnormality Cyclin D1 Protein Overexpression

Some Disease\_May\_Have\_Molecular\_Abnormality Cyclin D1 Messenger RNA Overexpression

Some Disease\_May\_Have\_Molecular\_Abnormality Cyclin E Protein Overexpression

Some Disease\_May\_Have\_Molecular\_Abnormality Beta Catenin Gene Mutation

Some Disease\_May\_Have\_Molecular\_Abnormality Transforming Growth Factor-Beta Overexpression

Some Disease\_May\_Have\_Molecular\_Abnormality Basic Fibroblast Growth Factor Overexpression

Some Disease\_May\_Have\_Molecular\_Abnormality Acidic Fibroblast Growth Factor Overexpression

Some Disease\_May\_Have\_Molecular\_Abnormality Aberrant DNA Methylation

Some Disease\_May\_Have\_Cytogenetic\_Abnormality del(1p)

Some Disease\_May\_Have\_Cytogenetic\_Abnormality del(4q)

Some Disease\_May\_Have\_Cytogenetic\_Abnormality del(5q)

Some Disease\_May\_Have\_Cytogenetic\_Abnormality del(8p)

Some Disease\_May\_Have\_Cytogenetic\_Abnormality del(13q)

Some Disease\_May\_Have\_Cytogenetic\_Abnormality del(16q)  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality del(17p)  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 8  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 20  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome X  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 6  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 18  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 3  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 16  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 10  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 17

#### **Fibrolamellar Hepatocellular Carcinoma**

All Disease\_Has\_Abnormal\_Cell Adenocarcinoma Cell with Eosinophilic Granular Cytoplasm  
 All Disease\_Has\_Abnormal\_Cell Polygonal Adenocarcinoma Cell with Eosinophilic Cytoplasm  
 All Disease\_Has\_Finding Trabecular Pattern

#### **Intrahepatic Cholangiocarcinoma**

All Disease\_Has\_Associated\_Anatomic\_Site Intrahepatic Bile Duct  
 All Disease\_Has\_Primary\_Anatomic\_Site Intrahepatic Bile Duct  
 All Disease\_Has\_Normal\_Tissue\_Origin Columnar Epithelium  
 All Disease\_Has\_Normal\_Cell\_Origin Columnar Cell  
 All Disease\_Has\_Abnormal\_Cell Adenocarcinoma Cell  
 Some Disease\_May\_Have\_Abnormal\_Cell Pleomorphic Adenocarcinoma Cell  
 Some Disease\_May\_Have\_Abnormal\_Cell Adenocarcinoma Clear Cell  
 Some Disease\_May\_Have\_Finding Thorotrast Exposure  
 Some Disease\_May\_Have\_Finding Abdominal Pain  
 Some Disease\_May\_Have\_Finding Malaise  
 Some Disease\_May\_Have\_Finding Weight Loss  
 Some Disease\_May\_Have\_Finding Multinodular Mass  
 Some Disease\_May\_Have\_Molecular\_Abnormality P53 Tumor-Suppressor Gene Inactivation  
 Some Disease\_May\_Have\_Molecular\_Abnormality KRAS Gene Amplification

#### **Hepatocellular Adenoma**

All Disease\_Has\_Associated\_Anatomic\_Site Liver  
 All Disease\_Has\_Normal\_Tissue\_Origin Hepatic Tissue  
 All Disease\_Has\_Normal\_Cell\_Origin Hepatocyte  
 All Disease\_Has\_Abnormal\_Cell Neoplastic Glandular Cell  
 Some Disease\_May\_Have\_Finding Necrotic Change  
 Some Disease\_May\_Have\_Finding Fibrosis  
 Some Disease\_May\_Have\_Finding Hemorrhagic Change

#### **Hepatic Carcinoid Tumor**

All Disease\_Has\_Associated\_Anatomic\_Site Liver  
 All Disease\_Has\_Primary\_Anatomic\_Site Liver  
 All Disease\_Has\_Normal\_Tissue\_Origin Hepatic Tissue  
 All Disease\_Has\_Normal\_Cell\_Origin Argentaffin Cell  
 All Disease\_Has\_Abnormal\_Cell Malignant Neuroendocrine Cell  
 All Disease\_Has\_Finding Neurosecretory Granule  
 Some Disease\_May\_Have\_Finding Insular Pattern  
 Some Disease\_May\_Have\_Finding Trabecular Pattern  
 Some Disease\_May\_Have\_Finding Glandular Pattern

#### **Childhood Liver Cancer**

All Disease\_Has\_Associated\_Anatomic\_Site Liver  
 All Disease\_Has\_Primary\_Anatomic\_Site Liver  
 All Disease\_Has\_Normal\_Tissue\_Origin Hepatic Tissue  
 All Disease\_Has\_Normal\_Cell\_Origin Hepatocyte  
 All Disease\_Has\_Abnormal\_Cell Malignant Epithelial Cell

#### **Hepatoblastoma**

Some Disease\_May\_Have\_Abnormal\_Cell Neoplastic Small Round Cell  
 Some Disease\_May\_Have\_Abnormal\_Cell Malignant Epithelial Large Cell  
 Some Disease\_May\_Have\_Abnormal\_Cell Neoplastic Spindle Cell  
 Some Disease\_May\_Have\_Finding Thrombocytosis  
 Some Disease\_May\_Have\_Finding Enlarging Abdomen



Some Disease\_May\_Have\_Finding Alpha Fetoprotein Increased  
 Some Disease\_May\_Have\_Finding Blood Alkaline Phosphatase Increased  
 Some Disease\_May\_Have\_Finding Fetal-Epithelial Differentiation  
 Some Disease\_May\_Have\_Finding Mesenchymal Differentiation  
 Some Disease\_May\_Have\_Finding Macrotrabecular Pattern  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Trisomy 2  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Trisomy 20  
 All\_Disease\_Is\_Stage Hepatoblastoma Stage

#### **Bile Duct Adenocarcinoma**

All Disease\_Has\_Associated\_Anatomic\_Site Bile Duct  
 All Disease\_Has\_Associated\_Anatomic\_Site Bile Duct  
 All Disease\_Has\_Normal\_Tissue\_Origin Columnar Epithelium  
 All Disease\_Has\_Normal\_Cell\_Origin Columnar Cell  
 All Disease\_Has\_Abnormal\_Cell Adenocarcinoma Cell

#### **Cholangiocarcinoma**

Some Disease\_May\_Have\_Abnormal\_Cell Pleomorphic Adenocarcinoma Cell  
 Some Disease\_May\_Have\_Abnormal\_Cell Adenocarcinoma Clear Cell  
 Some Disease\_May\_Have\_Finding Thorotrast Exposure  
 Some Disease\_May\_Have\_Finding Abdominal Pain  
 Some Disease\_May\_Have\_Finding Malaise  
 Some Disease\_May\_Have\_Finding Weight Loss  
 Some Disease\_May\_Have\_Finding Multinodular Mass  
 Some Disease\_May\_Have\_Molecular\_Abnormality P53 Tumor-Suppressor Gene Inactivation  
 Some Disease\_May\_Have\_Molecular\_Abnormality KRAS Gene Amplification

#### **Intrahepatic Cholangiocarcinoma**

All Disease\_Has\_Associated\_Anatomic\_Site Intrahepatic Bile Duct  
 All Disease\_Has\_Primary\_Anatomic\_Site Intrahepatic Bile Duct  
 All Disease\_Has\_Normal\_Tissue\_Origin Columnar Epithelium  
 All Disease\_Has\_Normal\_Cell\_Origin Columnar Cell  
 All Disease\_Has\_Abnormal\_Cell Adenocarcinoma Cell  
 Some Disease\_May\_Have\_Abnormal\_Cell Pleomorphic Adenocarcinoma Cell  
 Some Disease\_May\_Have\_Abnormal\_Cell Adenocarcinoma Clear Cell  
 Some Disease\_May\_Have\_Finding Thorotrast Exposure  
 Some Disease\_May\_Have\_Finding Abdominal Pain  
 Some Disease\_May\_Have\_Finding Malaise  
 Some Disease\_May\_Have\_Finding Weight Loss  
 Some Disease\_May\_Have\_Finding Multinodular Mass  
 Some Disease\_May\_Have\_Molecular\_Abnormality P53 Tumor-Suppressor Gene Inactivation  
 Some Disease\_May\_Have\_Molecular\_Abnormality KRAS Gene Amplification

#### **Hilar Cholangiocarcinoma**

All Disease\_Has\_Associated\_Anatomic\_Site Hepatic Duct  
 All Disease\_Has\_Primary\_Anatomic\_Site Hepatic Duct

#### **Extrahepatic Bile Duct Adenocarcinoma**

All Disease\_Has\_Associated\_Anatomic\_Site Extrahepatic Bile Duct  
 All Disease\_Has\_Primary\_Anatomic\_Site Extrahepatic Bile Duct



## **Breast Carcinoma Examples**

### **Breast Carcinoma**

All Disease\_Has\_Associated\_Anatomic\_Site Breast  
All Disease\_Has\_Primary\_Anatomic\_Site Breast  
All Disease\_Has\_Normal\_Tissue\_Origin Breast Tissue  
All Disease\_Has\_Normal\_Cell\_Origin Epithelial Cell  
All Disease\_Has\_Abnormal\_Cell Malignant Epithelial Cell  
Some Disease\_May\_Have\_Finding Breast Lump  
Some Disease\_May\_Have\_Finding Calcification  
Some Disease\_May\_Have\_Finding Microcalcification  
Some Disease\_May\_Have\_Molecular\_Abnormality EGFR Gene Amplification  
Some Disease\_May\_Have\_Molecular\_Abnormality FGFR1 Gene Amplification  
Some Disease\_May\_Have\_Molecular\_Abnormality c-myc Gene Amplification  
Some Disease\_May\_Have\_Molecular\_Abnormality FGFR2 Gene Amplification  
Some Disease\_May\_Have\_Molecular\_Abnormality CCND1 Gene Amplification  
Some Disease\_May\_Have\_Molecular\_Abnormality Cyclin D1 Protein Overexpression  
Some Disease\_May\_Have\_Molecular\_Abnormality Cyclin D1 Messenger RNA Overexpression  
Some Disease\_May\_Have\_Molecular\_Abnormality RB1 Tumor Suppressor Gene Inactivation  
Some Disease\_May\_Have\_Molecular\_Abnormality c-erbB2 Gene Amplification  
Some Disease\_May\_Have\_Molecular\_Abnormality c-erbB2 Protein Overexpression  
Some Disease\_May\_Have\_Molecular\_Abnormality c-erbB2 messenger RNA Overexpression  
Some Disease\_May\_Have\_Molecular\_Abnormality IGF2R Tumor Suppressor Gene Inactivation  
Some Disease\_May\_Have\_Molecular\_Abnormality TP53 Tumor Suppressor Gene Inactivation

### **Breast Adenocarcinoma**

All Disease\_Has\_Normal\_Tissue\_Origin Terminal Ductal Lobular Unit  
All Disease\_Has\_Normal\_Cell\_Origin Terminal Ductal Lobular Unit Cell  
All Disease\_Has\_Abnormal\_Cell Adenocarcinoma Cell  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 1q  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 6q  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 8q  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 17q  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 19q  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 20q  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of ChromosomeXq,  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 8p  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 13q  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 16q  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 17p  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 22q

### **Tubular Breast Carcinoma**

All Disease\_Has\_Finding Tubular Pattern  
Some Disease\_May\_Have\_Finding Desmoplastic Stroma Formation  
Some Disease\_May\_Have\_Finding Stellate Configuration  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 11q ATM Gene Locus  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 3p FHIT Gene Locus

### **Ductal Breast Carcinoma**

All Disease\_Has\_Abnormal\_Cell Ductal Carcinoma Cell

#### **Ductal Carcinoma In Situ of the Breast**

Some Disease\_May\_Have\_Abnormal\_Cell Adenocarcinoma Spindle Cell  
Some Disease\_May\_Have\_Abnormal\_Cell Adenocarcinoma Clear Cell  
Some Disease\_May\_Have\_Abnormal\_Cell Signet Ring Adenocarcinoma Cell  
Some Disease\_May\_Have\_Finding Nipple Discharge  
Some Disease\_May\_Have\_Finding Multifocal Lesion  
Some Disease\_May\_Have\_Finding Psammoma Body Formation  
Some Disease\_May\_Have\_Finding Paget Involvement  
Some Disease\_May\_Have\_Finding Cribriform Pattern  
Some Disease\_May\_Have\_Finding Micropapillary Pattern  
Some Disease\_May\_Have\_Finding Solid Pattern  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Polysomy 3

Some Disease\_May\_Have\_Cytogenetic\_Abnormality Polysomy 10  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Polysomy 17  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 1  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 18  
**Invasive Ductal Carcinoma, not Otherwise Specified**  
 Some Disease\_May\_Have\_Abnormal\_Cell Pleomorphic Epithelial Cell  
 Some Disease\_May\_Have\_Finding Firm Mass  
 Some Disease\_May\_Have\_Finding Trabecular Pattern  
 Some Disease\_May\_Have\_Finding Solid Pattern  
 Some Disease\_May\_Have\_Finding Syncytial Pattern  
 Some Disease\_May\_Have\_Finding Necrotic Change  
**Lobular Breast Carcinoma**  
 All Disease\_Has\_Abnormal\_Cell Lobular Carcinoma Cell  
 Some Disease\_May\_Have\_Abnormal\_Cell Pleomorphic Epithelial Cell  
 Some Disease\_May\_Have\_Finding Bilateral Mass  
 Some Disease\_May\_Have\_Finding Apocrine Metaplasia  
 Some Disease\_May\_Have\_Molecular\_Abnormality Loss of E-cadherin Expression  
 Some Disease\_May\_Have\_Molecular\_Abnormality CDH1 Tumor Suppressor Gene Inactivation  
**Lobular Carcinoma In Situ of the Breast**  
 Some Disease\_May\_Have\_Finding Multifocal Lesion  
 Some Disease\_May\_Have\_Finding Paget Involvement  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 16p  
**Invasive Lobular Breast Carcinoma**  
 All Disease\_Has\_Finding Single File Linear Pattern  
 All Disease\_Has\_Finding Fibrotic Stroma Formation  
**Mixed Lobular and Ductal Breast Carcinoma**  
 Some Disease\_May\_Have\_Molecular\_Abnormality Loss of E-cadherin Expression  
**Invasive Breast Carcinoma**  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality i(1)(q10),  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality i(8)(q10)  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality der(1;16)(q10;p10)  
**Tubular Breast Carcinoma**  
 All Disease\_Has\_Finding Tubular Pattern  
 Some Disease\_May\_Have\_Finding Desmoplastic Stroma Formation  
 Some Disease\_May\_Have\_Finding Stellate Configuration  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 11q ATM Gene Locus  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 3p FHIT Gene Locus  
**Invasive Ductal Carcinoma, not Otherwise Specified**  
 Some Disease\_May\_Have\_Abnormal\_Cell Pleomorphic Epithelial Cell  
 Some Disease\_May\_Have\_Finding Firm Mass  
 Some Disease\_May\_Have\_Finding Trabecular Pattern  
 Some Disease\_May\_Have\_Finding Solid Pattern  
 Some Disease\_May\_Have\_Finding Syncytial Pattern  
 Some Disease\_May\_Have\_Finding Necrotic Change  
**Invasive Lobular Breast Carcinoma**  
 All Disease\_Has\_Finding Single File Linear Pattern  
 All Disease\_Has\_Finding Fibrotic Stroma Formation  
**Female Breast Carcinoma**  
**Hereditary Female Breast Carcinoma**  
 Some Disease\_May\_Have\_Molecular\_Abnormality BRCA 1 Mutation  
**Male Breast Carcinoma**  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome X  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome Y  
 Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 5  
**Hereditary Male Breast Carcinoma**  
**Hereditary Breast Carcinoma**  
 Some Disease\_May\_Have\_Molecular\_Abnormality BRCA 2 Mutation  
**Hereditary Female Breast Carcinoma**  
 Some Disease\_May\_Have\_Molecular\_Abnormality BRCA 1 Mutation  
**Hereditary Male Breast Carcinoma**

### **Sporadic Breast Carcinoma**

Some Disease\_May\_Have\_Cytogenetic\_Abnormality Trisomy 7  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Trisomy 18  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Monosomy 6  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Monosomy 8  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Monosomy 11  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Monosomy 13  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Monosomy 16  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Monosomy 17  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Monosomy 22  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Monosomy X  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 17  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 6q  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 19  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 3p  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 11p  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 12q  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 1p  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Loss of Chromosome 9p  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 3q  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 6p  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 17q22-q24  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 3q  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 20q13  
Some Disease\_May\_Have\_Cytogenetic\_Abnormality Gain of Chromosome 7p

### **Breast Carcinoma Metastatic to the Skin**

All Disease\_Has\_Metastatic\_Anatomic\_Site Skin

## Other Examples Applying the Model

Note: Only selected roles/values are shown, to illustrate various aspects.

Most roles/values here would be inherited from parent categories, not asserted directly at this level.

### Metastatic Carcinoma to the Lung

Some	Disease_Has_Associated_Anatomic_Site	Lung
All	Disease_Has_Metastatic_Anatomic_Site	Lung
Some	Disease_Has_Primary_Anatomic_Site	Liver
Some	Disease_Has_Primary_Anatomic_Site	Prostate

### Prostate Carcinoma Metastatic to the Lung

Some	Disease_Has_Associated_Anatomic_Site	Prostate
Some	Disease_Has_Associated_Anatomic_Site	Lung
All	Disease_Has_Primary_Anatomic_Site	Prostate
All	Disease_Has_Metastatic_Anatomic_Site	Lung

### Gastrointestinal Stromal Tumor

All	Disease_Has_Primary_Anatomic_Site	Gastrointestinal Tract
All	Disease_Has_Normal_Cell_Origin	Interstitial Cell of Cajal
All	Disease_Has_Molecular_Abnormality	C-KIT Gene Rearrangement
All	Disease_Has_Molecular_Abnormality	KIT Receptor Tyrosine Kinase Protein (CD117) Overexpression

[one or both values]

Some	Disease_May_Have_Abnormal_Cell	Neoplastic Epithelioid Cell
Some	Disease_May_Have_Abnormal_Cell	Spindle Cell

[neither, one, or both values]

Some	Disease_May_Have_Cytogenetic_Abnormality	Monosomy of Chromosome 14
Some	Disease_May_Have_Cytogenetic_Abnormality	Loss of Chromosome 22

### Extraskelatal Myxoid Chondrosarcoma

All	Disease_Has_Normal_Cell_Origin	Chondrocyte
All	Disease_Has_Abnormal_Cell	Neoplastic Chondrocyte
All	Disease_Has_Normal_Tissue_Origin	Soft Tissue
All	Disease_Has_Finding	Non-Encapsulated Neoplasm
All	Disease_Has_Finding	Multinodular Pattern
All	Disease_Has_Finding	Chondromyxoid Stroma

[important typical value]

Some	Disease_Has_Finding	Pain
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[neither, one, or both values]

Some	Disease_May_Have_Abnormal_Cell	Neoplastic Epithelioid Cell
Some	Disease_May_Have_Abnormal_Cell	Rhabdoid Cell

[neither or one group of values]

#### Group 1

Some	Disease_May_Have_Cytogenetic_Abnormality	t(9;22)(q22;q12) Chromosomal Translocation
Some	Disease_May_Have_Molecular_Abnormality	Fusion Gene NR4A3/EWS Expression
Some	Disease_May_Have_Molecular_Abnormality	Fusion Protein NR4A3/EWS Expression

#### Group 2

Some	Disease_May_Have_Cytogenetic_Abnormality	t(9;17)(q22;q11) Chromosomal Translocation
Some	Disease_May_Have_Molecular_Abnormality	Fusion Gene NR4A3/RBP56 Expression
Some	Disease_May_Have_Molecular_Abnormality	Fusion Protein NR4A3/ RBP56 Expression

#### Group 3

Some	Disease_May_Have_Cytogenetic_Abnormality	t(9;15)(q22;q21)
Some	Disease_May_Have_Molecular_Abnormality	Fusion Gene NR4A3/TCF12 Expression
Some	Disease_May_Have_Molecular_Abnormality	Fusion Protein NR4A3/TCF12 Expression

### Lacrimal Gland Pleomorphic Adenoma

Some	Disease_Has_Associated_Anatomic_Site	Lacrimal Gland
All	Disease_Has_Primary_Anatomic_Site	Lacrimal Gland
All	Disease_Has_Normal_Tissue_Origin	Glandular Epithelium
All	Disease_Has_Normal_Tissue_Origin	Connective Tissue
All	Disease_Has_Normal_Cell_Origin	Glandular Cell
All	Disease_Has_Normal_Cell_Origin	Myoepithelial Cell (Basket Cell)
All	Disease_Has_Abnormal_Cell	Neoplastic Glandular Cell
All	Disease_Has_Abnormal_Cell	Neoplastic Stromal Cell
All	Disease_Has_Abnormal_Cell	Metaplastic Myoepithelial Cell
Some	Disease_May_Have_Finding	Squamous Metaplasia
Some	Disease_May_Have_Finding	Myxoid Stroma Formation
Some	Disease_May_Have_Finding	Chondromyxoid Stroma Formation

#### Add Role?

All	Disease_Has_Modifier	Metaplasia
All	Disease_Has_Modifier	Encapsulated